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EFFECT OF ETHANOL EXTRACT OF *PAULINIA PINNATA* LEAVES ON THE BLOOD PRESSURE OF CATS

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ABSTRACT

The effect of ethanol extract of the leaves of *Paulinia pinnata* was investigated on the blood pressure (BP) of normotensive adult cats. The LD_{50} value of the extract was first determined to ascertain its safety margin. LD_{50} value of 1190mg/kg, ED_{50} of 750mg/kg and therapeutic index of 1.85 suggest that the extract can be very toxic at higher doses. For the BP work, the cats were anaesthetized with pentobarbitone 40mg/kg via the intra peritoneal (IP) route. The femoral vein was cannulated for drug administration and carotid artery for blood pressure measurement. All drugs were dissolved in normal saline. On the anaesthetized cats, the ethanol extract of *Paulinia pinnata* leaves lowered the mean arterial blood pressure (MABP) by 74.9mmHg at a dose of 1.33×10^{-2} mg/kg. The lowering effect compared favourable with those of standard drugs (Acetylcholine and Histamine), which lowered MABP by 97.5 mmHg and 124.6mmHg respectively at the same dose of 1.33×10^{-4} mg/kg. The MABP lowering effect of the extract was appreciably blocked by a muscarinic antagonist (Atropine) and histaminergic antagonist (Promethazine), which suggests that the MABP lowering effect of the extract could have been achieved by binding to the numerous muscarinic and histaminergic receptors in the cardiovascular system. Thus, this experiment is suggestive of the mechanism of action of the extract.

KEYWORDS: *Paulinia pinnate*, Blood Pressure, Acetylcholine, Histamine, Muscarinic, Histaminergic, Atropine and Receptors

INTRODUCTION

Hypertension, a disorder of the cardiovascular system, characterized by sustained blood pressure higher than the generally accepted normal maximum level for a particular age group (Anne and Allison, 2001), is globally recognized as a major cause of death among adults due to associated complications including; coronary heart disease, stroke, sudden cardiac arrest, congestive heart disease, renal insufficiency, aneurysm, e.tc (Nosri *et al.,* 2001; Akinkughe, 2001; Oates and Brown, 2001).

It is reported that hypertension accounts for over 20% of deaths globally each year (Hart *et al.,* 1997). In view of the threats posed by this disease to man and the fact that effective orthodox remedies are yet to be found, means that traditional ways of treating the disease become imperative. The search for effective remedy to hypertension appears

promising because the tropics into which majority of Africa lies is host to about 2/3 of the world's flora and fauna and that means that a lot of medicinal plants can be found here for the curative and management of diseases (Sofowora, 1993).

Paulinia pinnata, popularly known as Yatsa biyar by the Hausas of Northern Nigeria is a tropical plant belonging to the family *sapindaceae*. It is a sub woody climber with tenderly small white flowers and scarlet capsular more or less three coupled fruit annually found as a regrowth vegetation in the savannah regions of tropical west Africa and grows in almost any kind of soil (Law, 1999). Traditionally, the leaves *of P. pinnata* were regarded as a terrible poison with a slow but surely fatal effect, although present day users have failed to corroborate this claim. The chief medicinal use in Africa seems to be an agent to stop bleeding, remedy for dysentery, arrest of threatened abortions, treatment of open wounds, diarrhea, tooth ache, opthalmia, aches and as a diuretic (Oliver, 1959). The claim that *P. pinnata* leaves have diuretic effect and can increase gastrointestinal motility raised the assumption that it may have parasympathetic activity and as such may be able to lower blood pressure. This served as motivation for this work. This study was therefore designed to determine the effect of the ethanol extract of *Paulinia pinnata* leaves on the blood pressure of cats.

MATERIALS AND METHODS

Collection and Preparation of Plant Material

The leaves of *P. pinnata* were collected from a herbalist based in terminus market, Jos Nigeria and was identified by Mr. Kareem Ibrahim of the Federal School of Forestry, Jos, as *Paulinia pinnata*, family *sapindaceae.* The collected leaves were air dried for 3 days after which they were pulverished to fine powder using a wooden mortar and pestle. 50g of the powder was subjected to soxhlet extraction for 48 hours at 78^0C using ethanol as a solvent. The extract was concentrated and dried at low temperature. The percentage yield of the final black crude extract was 36% (18.0g).

Acute Toxicity (LD_{50}) Study

An initial pilot study was conducted using 5 mice to determine the dose range of *P. pinnata* extract to be used for the study. For this pilot study 1000, 1500, 2000, 2500 and 3000mg/kg were administered, one dose on each mice. The death of 4 mice at the end of 24 hours (for doses 1500-3000mg/kg) served as basis for the LD_{50} dose design. For the LD_{50} 35 mice were divided into 7 groups of 5 mice each and each group was assigned a dose of the *P. pinnata* ethanol extract in the order, 500, 800, 1000, 1200, 1350, 1500 and 2000mg/kg by IP route. The mortality at the end of 24 hours in some groups was recorded and the LD_{50} value calculated to be 1190mg/kg using Karbar's method.

Effect of the Extract on the Blood Pressure of Anaesthetized Cats

Adult cats weighing 2.5-3.0kg were used for the study. They were maintained in the animal house of the Faculty of Medical Sciences, University of Jos, Jos, Nigeria, fed and allowed access to clean water *ad libitum.* They were anaesthetized with pentobarbitone (40mg/kg IP). Anesthesia was maintained using ether (via inhalation). The femoral vein was cannulated for drug administration. The trachea was also cannulated to facilitate respiration and the carotid artery was cannulated for blood pressure (BP) measurement. This cannula was connected to a pressure transducer coupled to a Polygraph (Washington 400md, 2C Oscillograph, Bioscience sheerness kent, U.K) which was loaded with recording paper. All drugs were dissolved in normal saline and administered via the femoral vein. Heparinised saline was also intermittently injected to prevent blood clotting. After the administration of any drug, the BP was allowed to stabilize before the next administration. The effect of the ethanol extract was measured and results were compared with the effects of the standard

drugs. The experiment was carried out in accordance with the Guidelines for Laboratory Procedures laid down by the University of Jos Ethics committee on Research as well as the internationally accepted principles regarding the care and use of animals for experimental techniques.

Drugs were administered in the following order

Acetylcholine

Histamine

Extract of *P. pinnata*

Atropin + Acetylcholine

Atropin + Extract

Promethazine + Histamine

Promethazine + Extract

Statistical Analysis

All values were expressed as mean ± SEM and results analyzed using student's t-test. P values <0.05 were considered statistically significant.

RESULTS

The effect of ethanol extract of *P. pinnata* leaves on the cat's blood pressure was evaluated. Results obtained (Table 1) showed that both Acetylcholine and Histamine as parasympathomimetic agents significantly (P<0.05) lowered the Mean Arterial Blood Pressure of cats when compared to basal values. The ethanol extract of *P. pinnata* leaves also significantly (P<0.05) lowered the Mean Arterial Blood Pressure with maximum fall (97.5mmHg) observed at a dose of 1.33x 10^{-2}mg/kg. In table 2, pretreatment with Atropine (6.6 x10^{-3}mg/kg) significantly blocked the effect of acetylcholine lowering the effect of Acetylcholine by 25.1mmHg. Promethazine (1.33 x 10^{-3}mmHg) also blocked the effect of Histamine (1.33 x 10^{-3}mg/kg) significantly. The effects of the extract was significantly blocked by Atropine in a graded manner, with maximum blockade noticed when 2.66 x 10^{-3}mg/kg was used to challenge the effect of 1.33 x 210^{-3}mg/kg of the extract. The MABP rose by 94.2mmHg due to the blocking effect of Atropine on the extract. The extract was also sufficiently blocked by Promethazine (1.33 x 10^{-3}mg/kg) a histaminergic receptor blocker, with a 63.3mmHg increase in MABP.

Table 1: Effects of Acetylcholine, Histamine and Extract of *P. pinnata* on the Mean Arterial Blood Pressure (MABP) of Cats

Drugs	Dose (mg/kg)	MABP ± SEM (mmHg)	Fall in Mean MABP (mmHg)
Acetylcholine	1.33 x 10^{-4}	71.2 ± 2.1	-97.5 ± 2.1
Acetylcholine	2.66 x 10^{-4}	179.9 ± 0.8	-22.8 ± 0.8
Acetylcholine	4.0 x 10^{-4}	160.4 ± 3.4	-11.9 ±3.4
Histamine	1.33 x 10^{-4}	49.4 ± 1.2	-124.6 ± 1.2
Extract of *P. pinnata*	1.33 x 10^{-2}	90.7 ± 4.1	-74.9 ±4.1
Extract of *P. pinnata*	2.7 x 10^{-2}	146.9 ± 3.6	-27.7 ± 3.6
Extract of *P. pinnata*	4.0 x 10^{-2}	154.5 ± 4.0	-20.1 ± 4.0

Table 2: Actions of Antagonists (Atropine Promethazine) on the Effects of Acetylcholine, Histamine and *P. pinnata* Extract on Cats Mean Arterial Blood Pressure (MABP)

Drugs	Dose (mg/kg)	MABP ± SEM (mmHg)	Rise in Mean MABP (mmHg)
Acetylcholine alone	1.33×10^{-4}	71.2 ± 2.1	-
Acetylcholine	1.33×10^{-4}	96.3 ± 1.8	25.8 ± 1.8 + +6.6 x 10-3
Atropine	6.6 x 10-3		
Histamine alone	1.33×10^{-4}	49.4 ± 1.6	
Histamine	1.33×10^{-4}	121.5 ± 2.0	72.1 ± 1.2
Promethazine	1.33×10^{-3}		
Extract of *P. pinnata* Alone	1.33×10^{-2}	90.7 ± 4.1	
Extract of *P. pinnata*	1.33×10^{-2}	144.4 ± 0.9	53.7 ± 0.9
Atropine	1.33×10^{-3}		
Extract of *P. pinnata*	1.33×10^{-2}	184.9 ± 1.3	94.2 ± 1.3
Atropine	2.66×10^{-3}		
Extract of P. pinnate	1.33×10^{-2}	154.0 ± 0.8	63.3 ± 0.8
Promethazine	1.33×10^{-3}		

DISCUSSIONS

The result of screening the effect of ethanol extract of *Paulinia pinnata* leaves on the blood pressure of anaesthetized cats showed that the extract caused a reduction in the Mean Arterial Blood Pressure (MABP) similar to the hypotensive response to Acetylcholine and Histamine. Acetylcholine achieved this blood pressure lowering effect by binding to muscarinic receptors in the cardiovascular system (Rang *et al.*, 2003; Woodrow, 1997) with muscarinic antagonist such as Atropine providing sufficient block while Histamine lowered MABP by binding to the cardiovascular histaminergic receptors with a Promethazine (a histaminergic antagonist) providing sufficient block (Goldstein et al.,1974; Katzung, 2007). The extract may have achieved its blood pressure lowering effect by binding to both muscarinic and histaminergic receptors in the cardiovascular system, since Atropine (a muscarinic antagonist) and Promethazine (a histaminergic antagonist) were able to sufficiently reduce the fall in MABP caused by the extract. Further studies are needed to identify the effect of this extract on blood lipid profile since this may reveal other mechanisms through which the extract exerts its hypotensive property.

CONCLUSIONS

In conclusion, the ethanol leaves extract of *P. pinnata* showed a hypotensive effect in cats which may have been mediated via the muscarinic and histaminergic receptors and raises hope in the numerous potential of herbs in the management of hypertension and future development of new drugs.

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